REMARKS

Status of the Claims

Pending claims

Claims 1 to 4, 6 to 22, and 31 are pending (claims 5, 23 to 30 and 32 to 40 were canceled in Applicants response of September 12, 2003).

Claims added in the instant amendment

Claims 41 to 69 are added in the instant amendment. Accordingly, after entry of the instant amendment, claims 1 to 4, 6 to 22, 31 and 41 to 69 will be pending and under consideration.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for methods for delivering nucleic acids to a heart can be found, inter alia, on pages 10 to 11, of the specification.

The Restriction Requirement

In the Restriction Requirement mailed August 13, 2003, the Patent Office alleged that the pending claims are directed to three separate and distinct inventions under 35 U.S.C. §121:

> Group I: Claims 23 to 27, drawn to a method for delivering a therapeutic dose of a gene expression cassette in a fluid selectively to a heart for sustained expression, wherein the gene of interest is a structural gene;
>
> Group II: Claims 28 to 30, drawn to a method for delivering a therapeutic dose of a gene expression cassette in a fluid selectively to a heart for sustained expression, wherein the gene of interest is a functional gene;
>
> Group III: Claims 32 to 40, drawn to a method for delivering a therapeutic dosc of a gene expression cassette in a fluid selectively to a heart for sustained expression, wherein the gene of interest is a mutated from of a gene.

The Patent Office alleged that claims 1 to 22 and 31 link the inventions of Groups I to III, and upon allowance of the linking claims the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination.

The Election

In response to the Restriction Requirement, Applicants elect Group III, claims 32 to 40, drawn to a method for delivering a therapeutic dose of a gene expression cassette in a fluid selectively to a heart for sustained expression, wherein the gene of interest is a mutated from of a gene, with traverse.

Patentably Distinct Species Requirement

The Patent Office alleged that the claims of Group I, claims 23 to 27, are directed to four patentably distinct species, set forth as species A to D, on page 4 of the Restriction Requirement mailed August 13, 2003.

The Patent Office alleged that the claims of Group II, claims 28 to 30, are directed to two patentably distinct species, set forth as species A and B, on page 5 of the Restriction Requirement.

The Patent Office further alleged that the claims of Group III, claims 32 to 40, are directed to seven patentably distinct species, set forth as species A to G, on pages 6 to 7 of the Restriction Requirement.

The Patent Office also alleged that claims 1 to 6 are generic to a plurality of disclosed distinct species of treatment methods requiring different steps for increasing dwell time of a fluid (in the heart), set forth as groups A to E, on page 7, of the Restriction Requirement.

The Species Election

In response to the Group III species requirement, Applicants elect species group C, a dominant negative form of PLB containing a mutation at amino acid 16 from serine (S) to glutamic acid (E), with traverse.

In response to the "treatment methods requiring different steps for increasing dwell time of a fluid" species requirement, Applicants elect group D, induction of complete or near-complete transient cardiac arrest, with traverse.

If the Patent Office withdraws the "patentably distinct species requirement" and has Applicants elect a species A to G, and these elected species are held to be allowable, Applicants are entitled to consideration (examination) of additional species; if all species are

held to be allowable, a generic claim should be allowed (MPEP §809.02(c); pg 800-50, 8th Edition, August 2001).

Reasons to reconsider and withdraw restriction requirement

Applicants respectfully request the Patent Office to reconsider and to withdraw the restriction requirement for the following reasons.

Applicants respectfully request the Patent Office to withdraw the restriction requirement and rejoin Groups I, II and III. Applicants also respectfully request the Patent Office to withdraw the "patentably distinct species" requirement as set forth on pages 4 to 7, of the Restriction Requirement mailed August 13, 2003. Applicants also respectfully request the Patent Office to withdraw, in part, the "patentably distinct species" requirement regarding "treatment methods requiring different steps for increasing dwell time of a fluid" as set forth on page 8, of the Restriction Requirement.

The instant invention is directed to novel methods for introducing nucleic acids into heart cells (cardiac myocytes). The methods of the invention are not limited to the introduction of any particular nucleic acid or gene. For example, the nucleic acids that are incorporated into viral vectors and introduced into heart cells using the methods of the invention can include nucleic acids (e.g., genes or cDNAs) encoding a protein (which can be any endogenous or heterologous protein, including structural proteins, "functional" proteins, "mutated" genes, and the like), an antisense RNA- or DNA- encoding gene or a nucleic acid encoding an siRNA, to name only a few examples.

The specification provides elegant examples as proof of principle that the novel methods of the invention are effective for the introduction of nucleic acids into heart cells. These examples include, inter alia, introduction of various "mutant" forms of nucleic acids encoding phospholamban (PLB), for example, dominant negative forms of PLB, including the allegedly "patentably distinct" species groups set forth on pages 5 to 7 of the Restriction Requirement. However, Applicants respectfully aver that the novelty of the methods of the invention is independent of which nucleic acid is selected to be introduced into a heart cell by a method of the invention. Thus, it is improper to define as a separate "patentably distinct" invention each different nucleic acid or gene used in the methods of the invention.

Additionally, Applicants respectfully aver that after a complete search directed to the novel methods of the invention (which are not limited to use of any particular nucleic acid or gene) it would not be an undue burden for the Patent Office to also do a complete search regarding making and using the methods of the invention with any particular nucleic acid or gene. Similarly, after a complete search directed to novel methods of the invention directed to using the methods of the invention with any particular nucleic acid or gene, it would not be an undue burden for the Patent Office to also do a complete search regarding making and using the novel methods of the invention which are not limited to use of any particular nucleic acid or gene.

Accordingly, Applicants respectfully request rejoining of Groups I, II and III and withdrawing of the "patentably distinct species requirement" as set forth on pages 5 to 7 of the office action.

Applicants also respectfully request the Patent Office to withdraw, in part, the "patentably distinct species" requirement regarding "treatment methods requiring different steps for increasing dwell time of a fluid" as set forth on page 8, of the Restriction Requirement. Applicants respectfully request rejoining of Groups D and E, as both Groups are directed to increasing dwell time of a fluid in a heart by decreasing the flow rate of the fluid in the heart by slowing (reversible bradycardia and near-complete cardiac arrest) or stopping (complete cardiac arrest) the flow of fluids (blood) in the heart. Applicants respectfully aver that after a search directed to the novel methods of the invention directed to increasing dwell time of a fluid in a heart by decreasing the flow rate of the fluid in the heart by slowing (reversible bradycardia and near-complete cardiac arrest) the flow of fluids (blood) in the heart, it would not be an undue burden for the Patent Office to also do a complete search regarding decreasing the flow rate of the fluid in the heart by stopping (complete cardiac arrest) the flow of fluids (blood) in the heart. Accordingly, Applicants respectfully request rejoin Groups D and E as set forth on page 8.

Applicant : Ken CHIEN
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CONCLUSION

Applicants have set forth distinct and specific errors in the restriction requirement and reasons for the Patent Office to reconsider and withdraw the restriction requirement. Accordingly, Applicants have preserved their right to petition the restriction to the Group Director under 37 CFR §1.144; see also MPEP §818.03(c); pg 800-60, 8th Edition, August 2001.

Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

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Gregory P. Einhorn
Reg. No. 38,440

Morrison & Foerster LLP
3811 Valley Centre Drive, Suite 500
San Diego CA 92130
direct dial 858 720 5133
fax 858 720 5125

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